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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

— *of inventorship (Rule 4.17(iv)) for US only*

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: CRH RESPONSIVE GENES IN CNS

(57) Abstract: The present invention relates generally to therapy and diagnosis of depression. In particular this invention relates to the polypeptides as well as to the polynucleotides encoding these polypeptides, wherein said polypeptides are shown to play a central role in mediating the endocrine response to corticotropin releasing hormone. These polypeptides and polynucleotides are useful in the diagnosis, treatment and/or prevention of depression.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/11792

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 C07K14/575

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, EMBL, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! 16 July 1999 (1999-07-16), XP002249222 retrieved from EBI Database accession no. AI842377 abstract --- -/--	26-31

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 February 2004	14. 05. 04

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Grosskopf, R

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BRUNSON K L ET AL: "Corticotropin releasing hormone downregulates CRF1 binding and induces CRF1 gene expression in hippocampus and cortex of the immature rat." SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 26, no. 1-2, 2000, pages Abstract No.-807.1, XP001153651 30th Annual Meeting of the Society of Neuroscience;New Orleans, LA, USA; November 04-09, 2000 ISSN: 0190-5295	
A	DA COSTA A P C ET AL: "Region-specific immediate-early gene expression following the administration of corticotropin-releasing hormone in virgin and lactating rats." BRAIN RESEARCH, vol. 770, no. 1-2, 1997, pages 151-162, XP001153650 ISSN: 0006-8993	
A	BAKSHI VAISHALI P ET AL: "Corticotropin-releasing hormone and animal models of anxiety: Gene-environment interactions" BIOLOGICAL PSYCHIATRY, ELSEVIER SCIENCE, NEW YORK, NY, US, vol. 48, no. 12, 15 December 2000 (2000-12-15), pages 1175-1198, XP001104031 ISSN: 0006-3223	
A	VAN GAALEN MARCEL M ET AL: "Effects of transgenic overproduction of CRH on anxiety-like behaviour." EUROPEAN JOURNAL OF NEUROSCIENCE, vol. 15, no. 12, June 2002 (2002-06), pages 2007-2015, XP002249220 June, 2002 ISSN: 0953-816X	
A	HOLSBOER FLORIAN: "The corticosteroid receptor hypothesis of depression." NEUROPSYCHOPHARMACOLOGY, vol. 23, no. 5, November 2000 (2000-11), pages 477-501, XP002249221 ISSN: 0893-133X	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/11792

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1 to 10 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-3, 26-31 (all partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: 1-3, 26-31 (all partially)

Method of diagnosing a CRH induced gene expression profile in an individual comprising obtaining a biological sample of said individual and determine the level of gene transcription of a gene comprising the nucleic acid sequence of SEQ ID NO: 1, the isolated polynucleotide sequence comprising SEQ ID NO: 1 vectors and host cells comprising said polynucleotide

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Inventions 2-29: Claims 1 to 26 (all partially)

Method of diagnosing a CRH induced gene expression profile in an individual comprising obtaining a biological sample of said individual and determine the level of gene transcription of a gene comprising the nucleic acid sequence of SEQ ID NO: 2 to 9, 11, 13, 15, 17, 19, 21, 23, 25-31, 32, 34, 36, 38, and 40; the isolated polynucleotide sequence comprising said SEQ ID NOs, vectors and host cells comprising said polynucleotide;
(a) Methods of diagnosing a CRH induced gene expression profile in an individual comprising obtaining a sample of said individual and determine the amount of at least one protein that modulates CRH signalling;
(b) Methods for identifying a compound capable to alter the CRH signalling response in a cell comprising contacting said cell with CRH in the presence or absence of said compound, determine the amount of at least one protein that modulates CRH signalling in said cell and compare the amount of said protein in the presence or absence of said compound
(c) Methods for identifying a compound capable to alter the CRH signalling response activity in a cell comprising contacting a cell which expresses at least one selected protein and compare the CRH response activity of said cell in the presence or absence of said compound;
wherein in the methods (a) to (c) the protein is selected from the proteins having the SEQ ID NOs: 10 and SEQ ID NOs: 12, 14, 16, 18, 20, 22, 22, 33, 35, 37, 39 and 41 (i.e. the proteins corresponding to the polynucleotides having SEQ ID NOs: 11, 13, 15, 17, 19, 21, 23, 32, 34, 36, 38 and 40)
